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10/686,083	10/15/2003	Narayan Sundararajan	42P13833D	7275

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EXAMINER
FORMAN, BETTY J

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/686,083	SUNDARARAJAN ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-8 and 10-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-8 and 10-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 5 July 2007 in which the Specification and claims 1, 8, 16, 19 were amended. All of the amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 12 March 2007 are withdrawn in view of the amendments.

Applicant's arguments have been thoroughly reviewed but are deemed moot in view of the amendments, withdrawn rejections and new grounds for rejection. New grounds for rejection, necessitated by the amendments, are discussed.

Claims 1-2, 5-8, 10-22 are under prosecution.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-2, 5-8, 10-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims have been amended to define the sensitivity of the detection unit and/or cantilever whereby a addition of a single nucleotide is detected. Applicant has pointed to numerous passages of the specification. However, none of the cited passages defines the

newly claimed detection unit or cantilever sensitivity. While the specification teaches detection of mass-labeled nucleotide addition based on differing mass labels (¶ 33-35 and Fig. 3-4). The specification does not define the detection as being related to the sensitivity of the detection unit or cantilever. The specification does not define any structural elements providing the claimed sensitivity so as to define the detection unit and/or cantilever over any other in the art.

Because the claims have been amended to describe sensitivity of the detection unit and/or cantilever and because the specification does not define what constitutes that sensitivity, the amendments are deemed new matter.

Claim Interpretation

4. The claims are drawn to an apparatus. The courts have stated that an apparatus must be defined by its structure, not function.

> The courts have stated that claims drawn to an apparatus must be distinguished from the prior art in terms of structure rather than function see *In re Danly*, 263 F.2d 844, 847, 120 USPQ 528, 531 (CCPA1959). "[A]pparatus claims cover what a device is, not what a device does." Hewlett-Packard Co. v. Bausch & Lomb Inc., 909 F.2d 1464, 1469, 15 USPQ2d 1525,1528 (Fed. Cir. 1990) (see MPEP, 2114).
>
> The instant claims define a plurality of chambers "for holding a plurality of different types of mass labeled nucleotides" .... "to introduce into the analysis chamber one type of mass labeled nucleotide at a time" .... "to sequentially cycle the plurality.....through the analysis chamber". These recitations define a use for the apparatus and reservoirs, but do not further define a structure of the apparatus or reservoir. Given the opinion of the courts, the amendments defining the reservoirs are interpreted as defining multiple chambers.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-2, 5-8 and 10-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baller et al (WO 01/33226, published 10 May 2001) in view of Williams et al (WO 99/57321, published 11 November 1999) and Warthoe (U.S. Patent Application Publication No. 2003/0054344, filed 30 August 2001) or Rothberg et al (U.S. Patent No. 6,274,320, issued 14 August 2001)

Regarding Claim 1, Regarding Claim 1, Baller et al disclose an apparatus for nucleic acid sequencing (page (page 13, lines 24-25).

The apparatus comprising a analysis chamber (Fig. 8) containing one or more cantilevers (#102) each comprising one or more covalently attached nucleic acid templates (thiol modified DNA attached to gold-coated cantilever, page 13, lines 9-15) wherein the cantilevers are responsive to deflection produced by changes in mass (i.e. addition of complementary sequence adds mass to the cantilever and causes deflection, page 13, lines 1-20), one or more reagent reservoirs in fluid communication with the chamber (i.e. input #112/output #113, Fig. 8), a detection unit operably coupled to the cantilever (PSD, #108) and a data processing and control unit "operably coupled" to the chamber, reservoirs and detection unit (PC #111, Fig. 8).

Baller et al further teach that detection of support-immobilized molecules using AMF have numerous disadvantages e.g. results are difficult to reproduce, strong dependence on and sensitivity to environmental parameters (page 1, lines 18-22) Baller et al further teach that cantilever-immobilized molecules do not suffer the same disadvantages due to the advantages

provided by the cantilever e.g. reliable recognition of molecules and reliable detection of properties in various environments (page 1, lines 23-26) thereby providing a very sensitive system with fast responses, suitable for mass production and re-use (page 4, lines 15-18).

Baller et al do not teach the device wherein having a reservoir with a polymerase or multiple reservoirs for sequential addition of nucleotides.

However, these elements were well known and routinely practiced in the art at the time the claimed invention was made as taught by Williams, Warthoe and Rothberg.

First, Williams teaches a similar device for nucleic acid sequencing (Abstract). The device comprising an analysis chamber comprising one or more double stranded nucleic acids (primer/template hybrid) wherein the nucleic acids are covalently attached to a support (page 11, lines 22-29) wherein the chamber is responsive to the addition of sequentially added and labeled nucleotides (page 19, lines 3-13), the apparatus further comprising one or more reagent reservoirs in fluid communication with the chamber, a detection unit operably coupled to the chamber and a data processing and control unit "operably coupled" to the chamber, reservoirs and detection unit and further comprising a polymerase within the chamber (Claims 27-42 and page 7, lines 6-13 and pages 8-11) and further teach the detection device having a sensitivity for detection of nucleotide incorporation (i.e. AFM, page 22, line 30-page 23, line 16)

Second, Warthoe teaches a similar device for sequencing (¶ 43). The apparatus comprising one or more cantilevers having a partially double stranded nucleic acid attached wherein the cantilevers detect mass change resulting from nucleotide addition/primer extension (¶ 43) and further teach the device comprises reagent reservoirs, channels and ports for selective addition to the device (¶ 128-129) and further comprises polymerase and labeled nucleotides (Example 2) thereby providing an inexpensive and integrated device for routine target detection as desired in the art (¶ 2 and 15).

Finally, Rothberg teaches a similar device for sequencing (Abstract). The apparatus comprising an analysis chamber having immobilized nucleic acids and polymerase and

reservoirs configured for sequential addition of mass labeled-nucleotides (Column 18, line 40-Column 19, line 35) and a data processing and control unit operably coupled to the device for detection and analysis of nucleotide addition (Column 30, lines 34-55). It is noted that the instant specification (¶ 74-76) broadly defines mass labeled nucleotides so as to encompass the labels of Rothberg.

Hence, all the structural elements of the claims were well known and routinely practiced in the art of nucleic acid sequencing.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made combine the teaching of Williams, Warthoe and Rothberg with that of Baller. Both Williams and Warthoe teach the cantilevered device comprising a polymerase and addition of labeled nucleotides and both clearly suggest a plurality of reservoirs for the nucleotides. And multiple reservoirs for sequential addition of nucleotides was also well known as taught by Rothberg. One of ordinary skill in the art would have been motivated to combine the teaches to provide the device of Baller with multiple reservoirs configured for sequential addition of nucleotides for the expected benefit of providing an integrated device as desired in the art (Warthoe, ¶ 2) and optimizing the controlled addition of reagents as provided by the sequential addition of reagents as taught by Rothberg (Column 19, lines 29-35).

Regarding Claim 2, Baller et al disclose the apparatus wherein the nucleic acids are about 10 nucleotides in length (e.g. 12 and 16 mer, page 12, lines 18-23).

Regarding Claim 5, Baller et al disclose the apparatus wherein the detection unit comprises a piezoresistor (page 7, lines 15-22).

Regarding Claim 6, Baller et al disclose the apparatus wherein the detection unit comprises a laser (page 7, lines 23-25).

Regarding Claim 7, Baller et al disclose the apparatus wherein the detection unit detects deflection of the cantilever (page 12, lines 12-17).

Regarding Claim 8, Baller et al disclose an apparatus comprising a analysis chamber (Fig. 8) containing one or more cantilevers (#102) each comprising one or more covalently attached nucleic acid templates (thiol modified DNA attached to gold-coated cantilever, page 13, lines 9-15) wherein the cantilevers are responsive to deflection produced by changes in mass (i.e. addition of complementary sequence adds mass to the cantilever and causes deflection, page 13, lines 1-20), a detection unit operably coupled to the cantilever (PSD, #108) and a data processing and control unit "operably coupled" to the chamber, reservoirs and detection unit (PC #111, Fig. 8). Baller et al further teach that detection of support-immobilized molecules using AMF have numerous disadvantages e.g. results are difficult to reproduce, strong dependence on and sensitivity to environmental parameters (page 1, lines 18-22) Baller et al further teach that cantilever-immobilized molecules do not suffer the same disadvantages due to the advantages provided by the cantilever e.g. reliable recognition of molecules and reliable detection of properties in various environments (page 1, lines 23-26) thereby providing a very sensitive system with fast responses, suitable for mass production and re-use (page 4, lines 15-18). Baller et al do not teach the device wherein having a reservoir with a polymerase or multiple reservoirs for sequential addition of nucleotides.

However, these elements were well known and routinely practiced in the art at the time the claimed invention was made as taught by Williams, Warthoe and Rothberg.

First, Williams teaches a similar device for nucleic acid sequencing (Abstract). The device comprising an analysis chamber comprising one or more double stranded nucleic acids (primer/template hybrid) wherein the nucleic acids are covalently attached to a support (page 11, lines 22-29) wherein the chamber is responsive to the addition of sequentially added and labeled nucleotides (page 19, lines 3-13), the apparatus further comprising one or more reagent reservoirs in fluid communication with the chamber, a detection unit operably coupled to the chamber and a data processing and control unit "operably coupled" to the chamber, reservoirs and detection unit and further comprising a polymerase within the chamber (Claims 27-42 and

page 7, lines 6-13 and pages 8-11) and further teach the detection device having a sensitivity for detection of nucleotide incorporation (i.e. AFM, page 22, line 30-page 23, line 16)

Second, Warthoe teaches a similar device for sequencing (¶ 43). The apparatus comprising one or more cantilevers having a partially double stranded nucleic acid attached wherein the cantilevers detect mass change resulting from nucleotide addition/primer extension (¶ 43) and further teach the device comprises reagent reservoirs, channels and ports for selective addition to the device (¶ 128-129) and further comprises polymerase and labeled nucleotides (Example 2) thereby providing an inexpensive and integrated device for routine target detection as desired in the art (¶ 2 and 15).

Finally, Rothberg teaches a similar device for sequencing (Abstract). The apparatus comprising an analysis chamber having immobilized nucleic acids and polymerase and reservoirs configured for sequential addition of mass labeled-nucleotides (Column 18, line 40-Column 19, line 35) and a data processing and control unit operably coupled to the device for detection and analysis of nucleotide addition (Column 30, lines 34-55). It is noted that the instant specification (¶ 74-76) broadly defines mass labeled nucleotides so as to encompass the labels of Rothberg.

Hence, all the structural elements of the claims were well known and routinely practiced in the art of nucleic acid sequencing.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made combine the teaching of Williams, Warthoe and Rothberg with that of Baller. Both Williams and Warthoe teach the cantilevered device comprising a polymerase and addition of labeled nucleotides and both clearly suggest a plurality of reservoirs for the nucleotides. And multiple reservoirs for sequential addition of nucleotides was also well known as taught by Rothberg. One of ordinary skill in the art would have been motivated to combine the teaches to provide the device of Baller with multiple reservoirs configured for sequential addition of nucleotides for the expected benefit of providing an integrated device as desired in

the art (Warthoe, ¶ 2) and optimizing the controlled addition of reagents as provided by the sequential addition of reagents as taught by Rothberg (Column 19, lines 29-35).

Regarding Claim 10, Baller et al disclose the apparatus wherein the data processing and control unit is a computer (PC #111, Fig. 8).

Regarding Claim 11, Baller et al disclose the apparatus wherein the detection unit comprises a laser and a position sensitive photo detector (page 15, line 28-page 16, line 1).

Regarding Claim 12, Baller et al disclose the apparatus wherein the detection unit comprises a piezoresistor (page 7, lines 15-22).

Regarding Claim 13, Baller et al disclose the apparatus wherein the nucleic acids are about 10 nucleotides in length (e.g. 12 and 16 mer, page 12, lines 18-23).

Regarding Claim 14, Baller et al disclose the apparatus further comprising an array of cantilevers (#102) wherein each cantilever is "associated with the same molecule".

The claims are given the broadest reasonable interpretation consistent with the broad claim language and specification wherein "associated with" is not defined. The apparatus of Baller has an array of cantilevers within a liquid cell having an inlet for fluid flow into the cell. The cell is used e.g. hybridization. Any molecule (e.g. buffer molecules) put into the cell via the inlet would be "associated with" each cantilever as claimed.

The courts have stated that claims must be given their broadest reasonable interpretation consistent with the specification *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997); *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969); and *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) (see MPEP 2111).

Regarding Claim 15, Baller et al disclose the apparatus further comprising an array of cantilevers (#102) wherein each cantilever is "associated with a different molecule" i.e. have different affinities for a target (page 8, lines 24-27; page 11, lines 14-20; and page 12, lines 18-23).

Regarding Claim 16, Baller et al disclose an apparatus comprising a analysis chamber (Fig. 8) containing one or more cantilevers (#102) each comprising one or more covalently attached nucleic acid templates (thiol modified DNA attached to gold-coated cantilever, page 13, lines 9-15) wherein the cantilevers are responsive to deflection produced by changes in mass (i.e. addition of complementary sequence adds mass to the cantilever and causes deflection, page 13, lines 1-20), a piezoresistor embedded at the fixed end of the cantilever (page 7, lines 15-22), a detection unit "operably coupled" to the piezoresistor to detect deflection (page 7, lines 15-22) and a data processing and control unit "operably coupled" to the chamber, reservoirs and detection unit (PC #111, Fig. 8).

Baller et al further teach that detection of support-immobilized molecules using AMF have numerous disadvantages e.g. results are difficult to reproduce, strong dependence on and sensitivity to environmental parameters (page 1, lines 18-22) Baller et al further teach that cantilever-immobilized molecules do not suffer the same disadvantages due to the advantages provided by the cantilever e.g. reliable recognition of molecules and reliable detection of properties in various environments (page 1, lines 23-26) thereby providing a very sensitive system with fast responses, suitable for mass production and re-use (page 4, lines 15-18).

Baller et al do not teach the device wherein having a reservoir with a polymerase or multiple reservoirs for sequential addition of nucleotides.

However, these elements were well known and routinely practiced in the art at the time the claimed invention was made as taught by Williams, Warthoe and Rothberg.

First, Williams teaches a similar device for nucleic acid sequencing (Abstract). The device comprising an analysis chamber comprising one or more double stranded nucleic acids (primer/template hybrid) wherein the nucleic acids are covalently attached to a support (page 11, lines 22-29) wherein the chamber is responsive to the addition of sequentially added and labeled nucleotides (page 19, lines 3-13), the apparatus further comprising one or more reagent reservoirs in fluid communication with the chamber, a detection unit operably coupled to the

chamber and a data processing and control unit "operably coupled" to the chamber, reservoirs and detection unit and further comprising a polymerase within the chamber (Claims 27-42 and page 7, lines 6-13 and pages 8-11) and further teach the detection device having a sensitivity for detection of nucleotide incorporation (i.e. AFM, page 22, line 30-page 23, line 16)

Second, Warthoe teaches a similar device for sequencing (¶ 43). The apparatus comprising one or more cantilevers having a partially double stranded nucleic acid attached wherein the cantilevers detect mass change resulting from nucleotide addition/primer extension (¶ 43) and further teach the device comprises reagent reservoirs, channels and ports for selective addition to the device (¶ 128-129) and further comprises polymerase and labeled nucleotides (Example 2) thereby providing an inexpensive and integrated device for routine target detection as desired in the art (¶ 2 and 15).

Finally, Rothberg teaches a similar device for sequencing (Abstract). The apparatus comprising an analysis chamber having immobilized nucleic acids and polymerase and reservoirs configured for sequential addition of mass labeled-nucleotides (Column 18, line 40-Column 19, line 35) and a data processing and control unit operably coupled to the device for detection and analysis of nucleotide addition (Column 30, lines 34-55). It is noted that the instant specification (¶ 74-76) broadly defines mass labeled nucleotides so as to encompass the labels of Rothberg.

Hence, all the structural elements of the claims were well known and routinely practiced in the art of nucleic acid sequencing.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made combine the teaching of Williams, Warthoe and Rothberg with that of Baller. Both Williams and Warthoe teach the cantilevered device comprising a polymerase and addition of labeled nucleotides and both clearly suggest a plurality of reservoirs for the nucleotides. And multiple reservoirs for sequential addition of nucleotides was also well known as taught by Rothberg. One of ordinary skill in the art would have been motivated to combine

the teaches to provide the device of Baller with multiple reservoirs configured for sequential addition of nucleotides for the expected benefit of providing an integrated device as desired in the art (Warthoe, ¶ 2) and optimizing the controlled addition of reagents as provided by the sequential addition of reagents as taught by Rothberg (Column 19, lines 29-35).

Regarding Claim 17, Baller et al disclose the apparatus further comprising a resistance measuring device (page 7, line 18).

Regarding Claim 18, Baller et al disclose the apparatus wherein the nucleic acids are about 10 nucleotides in length (e.g. 12 and 16 mer, page 12, lines 18-23).

Regarding Claim 19, Baller et al disclose an apparatus comprising a analysis chamber (Fig. 8) containing one or more cantilevers (#102) coated with a substance (e.g. gold layer, page 13, lines 13-15) each comprising one or more covalently attached nucleic acid templates (thiol modified DNA attached to gold-coated cantilever, page 13, lines 9-15) wherein the cantilevers are responsive to deflection produced by changes in mass (i.e. addition of complementary sequence adds mass to the cantilever and causes deflection, page 13, lines 1-20) a detection unit operably coupled to the cantilever (PSD, #108) and a data processing and control unit "operably coupled" to the chamber, reservoirs and detection unit (PC #111, Fig. 8).

Baller et al disclose the apparatus wherein the cantilevers function to detect biomolecule binding (page 9, lines 22-24) and are useful for determining base sequence analysis (page 13, lines 22-25) but they are silent regarding addition of polymerase to the analysis chamber. Baller et al do not teach the device wherein having a reservoir with a polymerase or multiple reservoirs for sequential addition of nucleotides.

However, these elements were well known and routinely practiced in the art at the time the claimed invention was made as taught by Williams, Warthoe and Rothberg.

First, Williams teaches a similar device for nucleic acid sequencing (Abstract). The device comprising an analysis chamber comprising one or more double stranded nucleic acids (primer/template hybrid) wherein the nucleic acids are covalently attached to a support (page

11, lines 22-29) wherein the chamber is responsive to the addition of sequentially added and labeled nucleotides (page 19, lines 3-13), the apparatus further comprising one or more reagent reservoirs in fluid communication with the chamber, a detection unit operably coupled to the chamber and a data processing and control unit "operably coupled" to the chamber, reservoirs and detection unit and further comprising a polymerase within the chamber (Claims 27-42 and page 7, lines 6-13 and pages 8-11) and further teach the detection device having a sensitivity for detection of nucleotide incorporation (i.e: AFM, page 22, line 30-page 23, line 16)

Second, Warthoe teaches a similar device for sequencing (¶ 43). The apparatus comprising one or more cantilevers having a partially double stranded nucleic acid attached wherein the cantilevers detect mass change resulting from nucleotide addition/primer extension (¶ 43) and further teach the device comprises reagent reservoirs, channels and ports for selective addition to the device (¶ 128-129) and further comprises polymerase and labeled nucleotides (Example 2) thereby providing an inexpensive and integrated device for routine target detection as desired in the art (¶ 2 and 15).

Finally, Rothberg teaches a similar device for sequencing (Abstract). The apparatus comprising an analysis chamber having immobilized nucleic acids and polymerase and reservoirs configured for sequential addition of mass labeled-nucleotides (Column 18, line 40-Column 19, line 35) and a data processing and control unit operably coupled to the device for detection and analysis of nucleotide addition (Column 30, lines 34-55). It is noted that the instant specification (¶ 74-76) broadly defines mass labeled nucleotides so as to encompass the labels of Rothberg.

Hence, all the structural elements of the claims were well known and routinely practiced in the art of nucleic acid sequencing.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made combine the teaching of Williams, Warthoe and Rothberg with that of Baller. Both Williams and Warthoe teach the cantilevered device comprising a polymerase and

addition of labeled nucleotides and both clearly suggest a plurality of reservoirs for the nucleotides. And multiple reservoirs for sequential addition of nucleotides was also well known as taught by Rothberg. One of ordinary skill in the art would have been motivated to combine the teaches to provide the device of Baller with multiple reservoirs configured for sequential addition of nucleotides for the expected benefit of providing an integrated device as desired in the art (Warthoe, ¶ 2) and optimizing the controlled addition of reagents as provided by the sequential addition of reagents as taught by Rothberg (Column 19, lines 29-35).

Regarding Claim 20-21, Baller et al disclose the substance is an alloy e.g. gold (page 13, lines 9-15).

Regarding Claim 22, Baller disclose the apparatus wherein the nucleic acids are coupled to the cantilever through a thiol group (page 13, lines 9-15).

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1-2, 5-8, 10-22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 15-17, 19-20, 29-30, 34-

37, 42-52 of copending Application No. 10/254,201 in view of Lindsay et al (U.S. Patent No. 5,750,989).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to an apparatus comprising cantilever structures, detection unit and data processing/control unit. The claim sets merely differ in that the instant claims define the cantilever as part of an analysis chamber. While the '083 claims do not require a chamber, cantilevers chambers were well known and routinely practiced in the art at the time the claimed invention was made as taught by Lindsay et al who teach that the chamber permits sample analysis within a controlled environment (Column 4, lines 12-34). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the chamber of Lindsay et al to the '083 apparatus for the expected benefit of environmentally controlled sample analysis as desired in the art (Lindsay et al, Column 4, lines 12-34). The claim sets further differ in that the '201 claims require a dielectric sphere, laser and objective lens. However, the instant claim language "comprising" encompasses the additional elements recited in the '201 claims. For these reasons, the claim sets are not patentably distinct.

This is a provisional obviousness-type double patenting rejection.

Response to Arguments

9. Applicant has provided no arguments regarding the above rejection. The rejection is maintained.

10. Claims 1-2, 5-8 and 10-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 24-46 of copending Application No. 10/705,389 as evidenced by Fritz et al (Science, 2000, 288: 316-318). Although the conflicting claims are not identical, they are not patentably distinct from each other because

both sets of claims are drawn to an apparatus comprising cantilever structures, detection unit and data processing/control unit. The claim sets merely differ in the arrangement of limitations within the claim sets and terminology used to define some elements. For example, the instant claims define the nucleic acids as being covalently attached to the cantilever while the '389 claims define the nucleic acid as being attached via a thiol group to a gold surface (e.g. Claims 44-45). Fritz et al define the thiol-gold attachment as covalent (page 318, right column ¶ 15). Therefore, the instantly claimed apparatus and that of the '389 claim set are not patentably distinct.

Response to Arguments

11. Applicant has not traversed the above rejection. The rejection is maintained.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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both sets of claims are drawn to an apparatus comprising cantilever structures, detection unit and data processing/control unit. The claim sets merely differ in the arrangement of limitations within the claim sets and terminology used to define some elements. For example, the instant claims define the nucleic acids as being covalently attached to the cantilever while the '389 claims define the nucleic acid as being attached via a thiol group to a gold surface (e.g. Claims 44-45). Fritz et al define the thiol-gold attachment as covalent (page 318, right column ¶ 15). Therefore, the instantly claimed apparatus and that of the '389 claim set are not patentably distinct.

Response to Arguments

11. Applicant has not traversed the above rejection. The rejection is maintained.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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Art Unit: 1634
August 2, 2007